Molecular BioSystems 2009 vol.5 N6, pages 612-628

Computational modelling suggests dynamic interactions between Ca $^{2+}$, IP3 and G protein-coupled modules are key to robust Dictyostelium aggregation

Valeyev N., Kim J., Heslop-Harrison J., Postlethwaite I., Kotov N., Bates D.
Kazan Federal University, 420008, Kremlevskaya 18, Kazan, Russia

Abstract

Under conditions of starvation, Dictyostelium cells begin a programme of development during which they aggregate to form a multicellular structure by chemotaxis, guided by propagating waves of cyclic AMP that are relayed robustly from cell to cell. In this paper, we develop and analyse a new model for the intracellular and extracellular cAMP dependent processes that regulate Dictyostelium migration. The model allows, for the first time, a quantitative analysis of the dynamic interactions between calcium, IP3 and G protein-dependent modules that are shown to be key to the generation of robust cAMP oscillations in Dictyostelium cells. The model provides a mechanistic explanation for the transient increase in cytosolic free Ca^{2+} concentration seen in recent experiments with the application of the calmodulin inhibitor calmidazolium (R24571) to Dictyostelium cells, and also allows elucidation of the effects of varying both the conductivity of stretch-activated channels and the concentration of external phosphodiesterase on the oscillatory regime of an individual cell. A rigorous analysis of the robustness of the new model shows that interactions between the different modules significantly reduce the sensitivity of the resulting cAMP oscillations to variations in the kinetics of different Dictyostelium cells, an essential requirement for the generation of the spatially and temporally synchronised chemoattractant cAMP waves that guide Dictyostelium aggregation.

http://dx.doi.org/10.1039/b822074c